



# Maternal Zinc Supplementation and Treadmill Exercise Mitigate Prenatal Stress-Induced Cognitive Deficits in Young Female Rat Offspring

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## ABSTRACT

**Introduction:** Pregnancy-related stresses have an enormous impact on the development of the embryo and can cause various kinds of neurological diseases later in life. The harmful impact on the morphology and function of the central nervous system, which can ultimately affect memory and learning abilities, is the most required of these alterations. Prenatal stress (PS) can generate neurological abnormalities that can be prevented or lowered with the use of physical or pharmacological therapies. The present study investigates the consequences of maternal zinc supplementation and prenatal physical activities on PS-induced cognitive and memory disorders in female rat offspring.

**Methods and Materials:** Pregnant rats were divided into five groups: control, stress, stress + exercise, stress + zinc, and stress + exercise + zinc. The stress groups were exposed to restrain stress for five consecutive days (Gestational days 15-19). The exercise and zinc groups were similarly exposed to stress and subjected to either forced treadmill exercise (30 min/daily), zinc sulfate (30 mg/kg/orally), or both throughout the pregnancy. On the 30th post-natal day, the Morris Water Maze (MWM) examined the female offspring's cognitive function. Newborns received four consecutive days of training in the maze before passing a test on the fifth day.

**Results:** The time spent finding the plate was used to evaluate learning, and the time spent in the target zone was used to evaluate memory. The results showed that the exercise and zinc groups took less time to find the plate and spent more time in the target area than the stress group. Accordingly, the escape latency significantly increased from  $11.8 \pm 1$  seconds in the control group to  $17.6 \pm 2$  seconds in the prenatally stressed group on training day four, indicating the impairment of spatial learning in these rats. Prenatal exercise and zinc supplementation completely reversed PS-induced learning impairments. Furthermore, prenatally stressed rats spent a significantly shorter time in the target zone ( $37.5 \pm 2.3$  s) than their non-stressed counterparts ( $43.9 \pm 2.4$  s). The time spent in the target zone for the offspring in the stress + exercise and stress + zinc groups significantly differed from the prenatally stressed rats and approached the control levels. The combined effects of exercise and zinc supplementation produced non-additive effects on cognitive impairments.

**Conclusion and Discussion:** Both prenatal exercise and zinc supplementation demonstrated beneficial effects on the learning and memory performance of the prenatally stressed offspring. These outcomes highlight the importance of zinc and physical activity in preventing PS-induced cognitive decline. However, it seems that zinc and exercise independently affected stress responses in the offspring, and as such, their combined effects did not yield more significant effects than either alone.

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